WO 2004/062551 PCT/BE2004/000002

98

CLAIMS

- 1. A polypeptide construct comprising:
- at least one single domain antibody directed against any of vWF, vWF A1 domain, A1
 domain of activated vWF, vWF A3 domain, gplb, or collagen.
 - 2. A polypeptide construct according to claim 1, further comprising at least one single domain antibody directed against one or more serum proteins.
- 3. A polypeptide construct according to claim 2 wherein said at least one serum protein is any of serum albumin, serum immunoglobulins, thyroxine-binding protein, transferring, or fibrinogen or a fragment thereof.
- 4. A polypeptide construct according to claims 2 and 3, wherein at least one single domain
 antibody directed against one or more serum proteins corresponds to a sequence represented by any of SEQ ID NO: 16 to 19 and 49 to 61.
 - 5. A polypeptide construct according to any of claims 2 to 4 corresponding to a sequence represented by any of SEQ ID NOs: 13 to 15 and 42 to 45.
 - 6. A polypeptide construct according to claim 1 to 5 wherein at least one single domain antibody is a humanised sequence.
- 7. A polypeptide construct according to claim 6 wherein at least one single domain antibody corresponds to a sequence represented by any of SEQ ID NOs: 38 to 41 and 42 to 45
 - 8. A polypeptide construct according to claim 1 corresponding to a sequence represented by any of SEQ ID NOs: 8 to 12, 20 to 22, 32 to 34, and 46 to 47.
- 9. A polypeptide construct according to any of claims 1 to 8 wherein at least one single domain antibody is a Camelidae VHH antibody.

25

- 10. A polypeptide construct according to any of claims 1 to 9 wherein at least one single domain antibody corresponds to a sequence represented by any of SEQ ID NOs: 1 to 7, 23 to 31, 35 to 37 and 62 to 65.
- 11. A polypeptide construct according to any of claims 1 to 10, wherein said single domain antibody is an homologous sequence, a functional portion, or a functional portion of an homologous sequence of the full length single domain antibody.
- 12. A polypeptide construct according to any of claims 1 to 11, wherein said polypeptide
 construct is a homologous sequence of said polypeptide construct, a functional portion thereof, of an homologous sequence of a functional portion thereof.
 - 13. A nucleic acid encoding a polypeptide construct according to any of claims 1 to 12.
- 15 14. A composition comprising a polypeptide construct according to any of claims 1 to 12 and at least one thrombolytic agent, for simultaneous, separate or sequential administration to a subject.
- 15. A composition according to claim 14 wherein said thrombolytic agent is any of
 staphylokinase, tissue plasminogen activator, streptokinase, single chain streptokinase,
 urokinase and acyl plasminogen streptokinase complex.
 - 16. A polypeptide construct according to any of claims 1 to 12, or a nucleic acid according to claim 13, or a composition according to claims 14 and 15 for use in the treatment, prevention and/or alleviation of disorders relating to platelet-mediate aggregation or dysfunction thereof.
 - 17. Use of a polypeptide construct according to any of claims 1 to 12, or a nucleic acid according to claim 13, or a composition according to claims 14 and 15 for the preparation of a medicament for the treatment, prevention and/or alleviation of disorders relating to platelet-mediate aggregation or dysfunction thereof.
 - 18. A polypeptide construct, nucleic acid or composition according to claim 16 or a use of a polypeptide construct, nucleic acid or composition according to claim 17 wherein said

5

10

disorders are any arising from arising from transient cerebral ischemic attack, unstable or stable angina, angina pectoris, cerebral infarction, myocardial infarction, peripheral arterial occlusive disease, restenosis, coronary by-pass graft, or coronary artery valve replacement and coronary interventions such angioplasty, stenting, carotid endarterectomy or atherectomy.

- 19. A polypeptide construct, nucleic acid or composition according to claim 16 or a use of a polypeptide construct, nucleic acid or composition according to claim 17 wherein said disorders are any of the formation of a non-occlusive thrombus, the formation of an occlusive thrombus, arterial thrombus formation, acute coronary occlusion, restenosis, restenosis after PCTA or stenting, thrombus formation in stenosed arteries, hyperplasia after angioplasty, atherectomy or arterial stenting, occlusive syndrome in a vascular system or lack of patency of diseased arteries.
- 20. A polypeptide construct, nucleic acid or composition according to claim 16 or a use of a polypeptide construct, nucleic acid or composition according to claim 17 wherein said disorder is plaque or thrombus formation in high sheer environments.
- 21. A polypeptide construct, nucleic acid or composition according to any of claims 16,18 to
 20 or a use of a polypeptide construct according to claim 17 to 20 wherein said polypeptide construct is administered intravenously, subcutaneously, orally, sublingually, topically, nasally, vaginally, rectally or by inhalation.
- 22. A composition comprising a polypeptide construct according to any of claims 1 to 12, 16,
 18 to 21 or a nucleic acid encoding said polypeptide construct, or a composition according to claims 14 and 15 and a pharmaceutically acceptable vehicle.
 - 23. A method of producing a polypeptide according to any of claims 1 to 12, 16, 18 to 21, comprising
- (a) culturing host cells comprising nucleic acid capable of encoding a polypeptide according to any of claims 1 to 12, 16, 18 to 21 under conditions allowing the expression of the polypeptide, and,
 - (b) recovering the produced polypeptide from the culture.

WO 2004/062551 PCT/BE2004/00002

101

- 24. A method according to claim 23, wherein said host cells are bacterial or yeast.
- 25. A method for treating invasive medical devices to prevent platelet-mediate aggregation around the site of invasion comprising the step of coating said device with a polypeptide construct according to claims 1 to 12.
- 26. An invasive medical device for circumventing platelet-mediate aggregation around the site of invasion, wherein said device is coated with a polypeptide construct according to claims 1 to 12.

10

5

- 27. A method of identifying an agent that modulates platelet-mediated aggregation comprising
- (a) contacting a polypeptide construct according to claims 1 to 12 with a polypeptide corresponding to its target, or a fragment thereof, in the presence and absence of a candidate modulator under conditions permitting binding between said polypeptides, and
- (b) measuring the binding between the polypeptides of step (a), wherein a decrease in binding in the presence of said candidate modulator, relative to the binding in the absence of said candidate modulator identified said candidate modulator as an agent that modulate platelet-mediated aggregation.

20

30

- 28. A kit for screening for agents that modulate platelet-mediated aggregation according to the method of claim 27.
- 29. An unknown agent that modulates platelet-mediated aggregation identified according to25 the method of claim 27.
 - 30. A method of diagnosing a disease or disorder characterised by dysfunction of platelet-mediated aggregation comprising the steps of:
 - (a) contacting a sample with a polypeptide construct according to claims 1 to 12, and
 - (b) detecting binding of said polypeptide construct to said sample, and
 - (c) comparing the binding detected in step (b) with a standard, wherein a difference in binding relative to said sample is diagnostic of a disease or disorder characterised by dysfunction of platelet-mediated aggregation.

WO 2004/062551 PCT/BE2004/000002

- 31. A kit for screening for diagnosing a disease or disorder characterised by dysfunction of platelet-mediated aggregation according to the method of claim 30.
- 32. A kit according to claim 28 or 31 comprising a polypeptide construct according to any of claims 1 to 12.